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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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New York, NY 10036

EXAMINER

MARVICH, MARIA

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/084,388

Applicant(s)

KOPYTEK ET AL.

Examiner

Maria B Marvich, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 6/10/04.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33, 51 and 79-83 is/are pending in the application.
- 4a) Of the above claim(s) 32, 33, 51 and 80-83 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-31 and 79 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/25/02, 10/10/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to a response to a restriction requirement filed 6/10/04. Post-mailing of the restriction requirement, a preliminary amendment filed 2/25/02 has been identified in which claims 34-50 and 52-78 have been cancelled. Therefore, claims 1-33, 51 and 79-80 are pending. In an interview, applicants have confirmed that Group I without the cancelled claims should be examined in a first action on the merits (see the attached interview summary).

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-31, 33-50 and 79) in the reply filed on 6/10/04 is acknowledged. The traversal is on the ground(s) that Groups I-IV are not distinct. Specifically, applicants have argued that the proteins of Group II are identified through the disclosed methods of Group I and the cells of Group III and small molecules of Group IV are used in the methods of Group I. Furthermore, applicants argue that there is not a serious burden on the Examiner to examine Group I-IV because a search for art material to the patentability of any of the Groups would turn up prior art material to the patentability of the remaining claims.

Applicants' arguments have been considered but are not persuasive because as detailed in the restriction requirement mailed 5/5/04, the proteins are related as products and process of making but are distinct as the product as claimed can be made by another and materially different process i.e. synthetically (see MPEP (§ 806.05(f)). The cells of Group III and the small molecules of Group IV are related as product and process of use with the methods of Group I. The inventions of Group I and III and IV can be shown to

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be distinct as the products as claimed can be used in a materially different process of using that product i.e. (see MPEP § 806.05(h)). Therefore, while the inventions of Group II-IV are related to Group I, the inventions are distinct.

As to search burden, the different groups comprise divergent subject matter for which a search for art pertaining to each group is not coextensive. For example, a search for art pertaining to a given proteins is not coextensive with a search for art for a method of identifying a protein from a pool of candidates. A search for art pertaining to small molecules is not coextensive with a search for art pertaining to a method of identifying a protein from a pool of candidates. Nor is a search for art pertaining to transgenic cells comprising small molecules, sequences that encodes an enzyme, first and second fusion proteins and reporter genes coextensive with a method of identifying a protein from a pool of candidates.

The requirement is still deemed proper and is therefore made FINAL. Claims 34-50 and 52-78 have been cancelled, claims 23-33, 51 and 80-83 have been withdrawn. Therefore, claims 1-31 and 79 are under examination in this application.

Information Disclosure Statement (IDS)

Information Disclosure Statements filed 2/25/02 and 10/10/03 have been identified and the documents considered. The signed and initialed PTO Form 1449s have been mailed with this action. Documents listed on the IDS as Exhibit 39, 45 and 46 are US applications invented by others. The documents have been considered but have been crossed out so that they will not appear on the face of an issued patent. The Document

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listed as Exhibit 36 is an International Search Report, which is also not considered to be a published reference. Therefore, this listing has been crossed out as well.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, the letter stating that the contents of the sequence listing and the CRF are the same must state that there is no new matter by the submission of the sequence listing and CRF. A new sequence listing, CRF and letter stating that there is no new matter and that the contents of the sequence listing and CRF are the same is required.

Specification

The abstract is objected to as it exceeds 150 words.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited.

The disclosure is objected to because of the following informalities: blank sections occur on page 9, 20 and 27. It is unclear if these blank sections reflect deleted

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matter or if the blanks exist to specifically format the specification. Appropriate correction is required.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 7-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 69- 79 of copending Application No. 10/705,644. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite methods of screening for enzymes that catalyze bond formation between a first and second substrate thus forcing dimerization of two fusion proteins. The instant claims recite that the first and second substrates are components of larger molecules, the first

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fused to a receptor recognition domain and the second fused to a transcriptional activator, while application 10/705,644 recites that the first and second compounds (substrates) are introduced individually into the cell and form an interaction with each of the dimerizing fusion proteins. It would have been obvious to one of ordinary skill at the time of the invention was made to substitute the fusions comprising the first and second substrates of the instant invention with individual first and second compounds as in application 10/705,644 because the instant invention teaches that it is within the ordinary skill of the art to catalyze bond formation using fusion proteins comprising substrates of the bond formation and because application 10/705,644 teaches that it is within the ordinary skill of the art to catalyze bond formation between two substrates within a cell. One would have been motivated to do so in order to receive the expected benefit of the substrates, which can be quite small, fused to larger molecules that are components of the screening complex. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Additionally, if a patent resulting from the instant claims was issued and transferred to an assignee different from the assignee holding a patent from 10/705,644, then two different assignees would hold a patent to the claimed invention of 10/705,644, and thus improperly there would be possible harassment by multiple assignees.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-31 and 79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 79 are vague and indefinite in that the metes and bounds of “a moiety that contains the first substrate” are unclear. Moiety is defined alternatively as one of two equal parts or a functional group. It is unclear how either of these definitions can describe something that “contains the first substrate”.

Claim 1 is vague and indefinite in that the metes and bounds of “permitting the dimeric molecule to bind to the first fusion protein” are unclear. It is unclear what is required of “permitting” the binding reaction to occur.

Claim 1 is vague and indefinite in that the metes and bounds of “selecting which cell expresses the reporter gene” are unclear. The reporter gene is only in “a cell” and accordingly, there is only one cell expressing the reporter gene. It is unclear from what the cell is selected.

Claim 2 is vague and indefinite in that the metes and bounds of “the protein” of claim 1 are unclear. There are three proteins described in claim 1 and therefore, it is unclear if “the protein” is the first fusion protein, the second fusion protein or the candidate protein.

Claim 4 is vague and indefinite in that the metes and bounds of “a preparation of random proteins” are unclear. It is unclear if the “preparation of random proteins” is

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present in the cell or the preparation serves as a source of individual proteins that are each provided to the cell. Furthermore, it is unclear to what the term “random” refers, the term “random” is a relative one for which neither the specification nor the prior art prescribes a standard meaning thus it is unclear if this “random protein” is in addition to the “candidate protein” or is the same.

Claim 4 is vague and indefinite in that the metes and bounds of “competitive enzymatic bond formation” are unclear. It is unclear what is competing against what and how “competitive enzymatic bond formation” is measured such that the protein with enhanced enzymatic activity is identified.

Claim 79 is vague and indefinite in that the metes and bounds of means of inserting DNA encoding a receptor domain into the second vector are unclear. The second vector does not encode the DNA binding domain rather a fusion exists between the DBD and the receptor domain. Therefore, it is unclear how means of inserting the receptor domain into the second vector are to be used in step f) of the instant invention.

Claim 79 is vague and indefinite in that the metes and bounds of means of inserting DNA encoding a second substrate into the first vector are unclear. The first vector does not encode the transcriptional activator and rather a fusion exists between the transcriptional activator and the second substrate. Therefore, it is unclear how means of inserting the receptor domain into the first vector are to be used in step g) of the instant invention.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 6-31 and 79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention recites a method of identifying which protein from a pool of proteins has catalyzed bond formation between a first and second substrate. A cell is provided which contains a receptor moiety domain fused to a DNA binding domain and a second substrate fused to a transcriptional activator and a candidate protein that can catalyze bond formation between the second substrate and a first substrate. The first substrate fused to a receptor moiety is introduced into the cell and reporter gene activity is used as a measure of enzyme catalysis. The invention recites a broad genus of host cells that can be used to perform the instant method.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

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The instant invention is based upon components of yeast hybrid screens and chemically induced dimerization (CID) systems. Applicants exemplify the instantly recited enzyme assisted CID (eaCID) in yeast cells. As an essential element, the invention requires generation of a cell that contains components to be used in the screen. This requires transformation of the cells with a complex assortment of fusion proteins encoded on vectors that are specific to the cell type. The invention has not been so disclosed in words or drawings such that a person of skill in the art would conclude that applicants were in possession of the instantly recited genus of host cells transformed with a receptor moiety domain fused to a DNA binding domain and a second substrate fused to a transcriptional activator and a candidate protein that can catalyze bond formation between the second substrate and a first substrate and a second substrate fused to a receptor moiety and reporter gene. Given the diversity of requirements that must be adapted to the diverse nature of cells, and the inability to determine which combinations of components will be active in the different cells, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1, 2 and 5-17 are rejected under 35 U.S.C. 103(a) as being obvious over Cornish (US 2004/0106154; see entire document).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Applicants claim a method of identifying which protein from a pool of proteins has catalyzed bond formation between a first and second substrate. A cell is provided which contains a receptor moiety domain fused to a DNA binding domain and a second substrate fused to a transcriptional activator and a candidate protein that can catalyze

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bond formation between the second substrate and a first substrate. The first substrate fused to a receptor moiety is introduced into the cell and reporter gene activity is used as a measure of enzyme catalysis.

Cornish teaches a method for the identification of protein with the ability to catalyze bond formation comprising the steps of providing a cell with a pair of fusion proteins, which upon dimerization activates a cellular readout. The cell is further provided with a first and second compound each capable of binding to one of the pair of fusion proteins. Bond formation results in dimerization of the pair of fusion proteins (see e.g. paragraph 002100024). Bond formation is indicated by gene transcription such as by LacZ (see e.g. paragraph 0100). Cells include bacterial, yeast or mammalian and the fusion proteins may be glucocorticoid receptor and B42 and DHFR such as from E. coli and LexA pr vice versa (see e.g. paragraphs 0093 through 0098). The proteins are encoded by DNA (see e.g. paragraph 0046). Pools of proteins are generated by combinatorial techniques (see paragraph 0005). Steps are repeated iteratively to identify a molecule capable of competitively binding the target proteins (See e.g. paragraph 0146).

It would have been obvious to one of ordinary skill at the time of the invention was made to substitute the fusions comprising the first and second substrates of the instant invention with individual first and second compounds as in Cornish because the instant invention teaches that it is within the ordinary skill of the art to catalyze bond formation using a fusion protein comprising a substrate of the bond formation and because Cornish teaches that it is within the ordinary skill of the art to catalyze bond formation between two substrates within a cell. One would have been motivated to do so

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in order to receive the expected benefit of the substrates, which can be quite small, fused to larger molecules that are components of the screening complex. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


GERRY LEFFERS
PRIMARY EXAMINER

Maria B Marvich, PhD
Examiner
Art Unit 1636

July 8, 2004